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Sudan University of Science and Technology
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Assessment Of Serum Total Cholesterol Level and Aspartate Transaminase Activity Among Sudanese Cigarette Smokers

(Study in Khartoum State)

تقويم مستوى الكلسترول الكلى ونشاط انزيم الاسبارتيت ترانزامينيز فى مصل المدخنين السودانين (دراسة فى ولاية الخرطوم(

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بِسْمِ اللّهِ الرَّحْمَنِ الرَّحِيمِ

قال الله تعالى

لا يُكَلِّفُ اللَّهُ نَفْساً إِلَّا وُسْعَهَا لَهَا مَا كَسَبَتْ وَعَلَيْهَا مَا اكْتَسَبَتْ رَبَّنَا لا تُؤَاخِذْنَا إِنْ نَسِينَا أَوْ أَخْطَأْنَا رَبَّنَا وَلا تَحْمِلْ عَلَيْنَا إِصْراً كَمَا حَمَلْتَهُ عَلَى الَّذِينَ مِنْ قَبْلِنَا رَبَّنَا وَلا تُحَمِّلْنَا مَا لا طَاقَةَ لَنَا بِهِ وَاعْفُ عَنَّا وَاغْفِرْ لَنَا وَارْحَمْنَا أَنْتَ مَوْلانَا فَانْصُرْنَا عَلَى الْقَوْمِ الْكَافِرِينَ

صدق الله العظيم

سورة البقرة الآية: 286

Dedication

To my lovely parents

To my sisters and brothers

To all m y friends

To all my teachers

Acknowledgments

My first thankful is to Allah all of his affluences and my special thank to my supervisor **Dr.Mohammed Abd ELrahim AbdAllah** for his precious advice .

Thanks and regards were extended to clinical chemistry staff in Sudan University and finally all our thanks to everyone who supported and helped us through this study.

Abstract

This study was carried out to measure serum total cholesterol level and Aspartate transaminase (AST)activity in the blood male of Sudanese with cigarette smokers.

Fifty samples were collected from cigarette smokers without any disease in period between May –September 2013.

Fifty smokers between the age 18-86 years and with duration ranging 2-35years .two and half of blood samples were taken from these cigarette smoker's as well as 50 male non smokers also in this study roll all the participant were randomly select present social status.

Samples were collected from non cigarette smoker's subject as control group to measure serum total cholesterol level by using colorimeter and Aspartate transaminase (AST) activity By using sepectrophotometer All results were analyzed using statistical of package social science) SPSS(computer program.

The study showed that a significant elevation of serum total cholesterol level in cigarette smokers (211±8.3) mg/dl when compared to non cigarette smokers (154+5.4) mg/dl with P.value (0.008) The study also showed that Aspartate transaminase (AST)activity was significant ly increased in blood of smokers compared to control being (38±10) µ/l (23±5.4) µ/l with P.value (0.001) .

The study indicates that the duration of cigarette smokers has significantly increased the level of cholesterol and Aspartate transaminase(AST) activity with p.value (0.007) .

The study indicates that the number of cigarette /day has significant difference between serum total cholesterol level. Mean 2-10 cigarette/day (209±5.7) mg/dl more than 11cigarette /day (224±8.4) mg/dl
p.value =0.0000

The study indicates that serum total cholesterol level is not significantly affected by age of cigarette smokers there is no different in value in total cholesterol level between two age group in this study Mean in 18- 45 years (211±5.5) mg/dl 46- 85years (209±4.1) mg/dl with p.value (0.34) .

The enzyme Asparate transaminase (AST)activity was no significant differ the value was regret to duration of smoker age the smoker number cigarette smokers.

Person correlation show that there was significant weak positive correlation between the duration of cigarette smokers and the level of Serum cholesterol and r = 0.065 with p.value (0.65) no significant between duration and total cholesterol level cigarette smokers also no correlation between age of smokers number of smoker .

Aspartate transaminase activity in other hand also show no correlation of statistical significance with duration of smoker ,age smoked and number of smokers the out came of this study total cholesterol level and Aspartate transaminase (AST)activity enzyme significance increase in blood of the smokers with remarkable affect duration of smoker and number of cigarette smoked.

Condition that may increase the risk of cardiovascular disease and atherosclerosis.

□□□□□□□

إجريت هذه الدراسة لقياس معدل الكلسترول الكلي ونشاط انزيم الاسبارتيت ترنزامينيز في دم المدخنين و قد تمت دراسة ٥٠ مدخن سوداني في ولاية الخرطوم في الفترة ما بين مايو واكتوبر ٢٠١٣

اخذت عينات الدم اثنين ونصف مل من ٥٠ ذكور مدخنين سجار بين الاعمار ١٨- ٨٦ سنة وفترة تدخين اثنين الي خمس وثلاثين سنة اختيرت خمسين مدخن سجارمن المجتمع عشوائية وكذلك ٥٠ عينة من ذكور غير مدخنين سجاراستخدمت كمحكم وتم قياس مستوى الكلسترول الكلي ونشاط انزيم الاسبارتيت ترنزامينيز لهذه العينات باستخدام جهاز قياس الطيف المرئي وجهاز قياس الطيف غير المرئي كل النتائج حللت باستخدام برنامج الكمبيوتر الحزمه الاحصائيه للعلوم ألاجتماعيه

نتائج هذه الدراسة اظهرت ان هنالك زيادة معنوية ذو دلالة احصائية في مستوي الكلسترول الكلي ونشاط أنزيم الاسبارتيت ترنزامينيزعند المدخنين مقارنة بالمجموعة الضابطة

(٨,٣٢١١±) مليجرام/دسلتر (٥,٤±١٥٤) مليجرام/دسلتر و(مستوى المعنوية=٠,٠٠٨) علي التوالي وأيضا هنالك تأثير واضح في نشاط انزيم الاسبارتيت ترنزامينيزعند المدخنين مقارنة بالمجموعة الضابطة(٣٨± ١٠(وحدة/لتر) ٢٣ ±٥ (وحدة/لتر و(مستوي المعنوية = ٠٠١.٠) على التوالي

كما اظهرت الدراسة انه يوجد فرق ذو دلالة احصائية على تركيز الكلسترول الكلي مقارنة بفترة التدخين (مستوى المعنوية = ٠,٠٠٧)

اوضحت الدراسة انه يوجد فرق ذو دلالة احصائية على تركيز الكلسترول مقارنة بعدد السجائر في اليوم عند المدخنين ٢-١٠سجارة/اليوم(٢٠٩± ٥,٧)مليجرام/دسلتر اكثر من ١١ سجارة /اليوم

(٢٢٤±٤,٨) مليجرام/دسلتر و)مستوي المعنوية ٠,٠٠٠(

اوضحت الدراسة انة ليس هنالك تأثير للأعمار المدخنين على مستوى الكلسترول الكلي في الدم

١٨-٤٥سنة)٢١٣ ± ٥,٥) مليجرام/دسلتر ٤٦ -٨٦ سنه (٢٠٩± ٤,١) مليجرام/دسلتر و

(مستوى المعنوية=٠,٣٤) اوضحت الدراسة ان نشاط انزيم الاسبارتيت ترنزامينيز لا يوجد فرق ذو دلالة احصائية فى فترة التدخين ,اعمار المدخنين وعدد السجارفى اليوم .

معامل بيرسون للارتباط وجد انة يوجد علا قة معنوية ضعيفة بين فترة التدخين وعدد السجار معامل بيرسون للارتباط =**٠ر٠٦٥** (مستوى المعنوية =(٠,٦٥) معامل بيرسون للارتباط =**٠ر١٢٩**

(مستوى المعنوية = ٣٧ **٠ر**) علي التوالي .لايوجد فرق ذو دلالة احصائية بين فترة التدخين ومستوى الكلسترول ولا علا قة بين عمر المدخن السجار.

وأيضا نشاط أنزيم الاسبارتيت ترنزاميز لا يوجد علا قة معنوية بين عددالسجار,عمرالمدخن وفترة التدخين,

نتائج الدراسة اوضحت ان مستوى الكلسترول الكلى ونشاط انزيم الاسبارتيت ترنزاميز معنوية يذيد عند مدخنين السجار يتاثر بعدد السجارفى اليوم وفترة التدخين.هذة الظروف تذيد الخطور بامراض القلب وتصلب الشرايين.

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Abbreviations

AMI	Acute MycardiaInfarction
AspAT	Aspartate AminoTranferase
AST	Aspartate Transaminase
cAST	Cytosolic Aspartate
CHD	Coronary Heart Disease
CoA	Coenzyme A
EC	Enzyme Commission
FFA	Free fatty Acid
GLU	Glutamate
HDL	High Density Lipoprotein
HMG	Hydroxy 3Methl Glatryl
IDL	Intermediate Density Lipoprotein
IHD	Ischemic Heart Disease
LDL	Low Density Lipoprotein
m AST	mitochondrial Aspartate
Mg/dl	Milli gram per diluter
µmol/dl	Micro mol per diluter
NAD	Nicotinamide AdenineDinucleotide
NADH	Nicotinamide adeninedinucleotide phosphate
NEFA	Non esterifies Fatty Acid
PMP	Pridoxamine phosphate
PLP	Pridoxal phosphate
r	Correlation
RHD	Rheumatic Heart Disease
SD	Standard Deviation
SGOT	Seum Glutamic Transaminase
TC	Total Cholesterol
VLDL	Very Low Density Lipoprotein
WHO	World Health Organization

CHAPTER ONE

introduction

1.Chapter one

1.1 introduction

Smoking is practice where a substance is burned and the smoke tasted or inhaled .this is primarily done as from of recreational drug use

(Surgeon 2004)as of 2000 1.22 billion people worldwide practice smoking assuming no change in prevalence it is predicted that 1.45 billion people will smoke in2010 and 1.5 to 1.9 billion in 2025 (Guindon 2003)in 2004 the WHO projected 58.8 billion death to occur globally from which 5.4 million are tobacco attributed and 4.9 million as of2007 (WHO 2004).

Worldwide the effects of smoking are estimated to kill 3 million per year. This contrast with 0.2 million in 1950 and projections for 2025 of 10 million (Bertteridge &morel 1998).

Smoking is considered as major cardiovascular risk factor and is one of the main avoidable causes death in the world (Murray *etal* 1998) it is also considered as an important factor in the stimulation if the development of atherosclesis (Bereson *et.al* 1997) smoking act synergist calls with the risk factor elevated blood fat levels high blood pressure to greatly increase the risk of CVD (health care 2005).

Statistically coronary artery disease to occur more frequently and at earlier age in the person who smokes much than non smoker likewise the mortality rate is higher among younger persons with coronary disease who are non smokers(Grace *etal* 1998).

Increase total cholesterol value are associated a progressively escalating risk of atherosclerosis and coronary artery disease (Tetiz 1991).

Smoking in different forms is a major risk factor for atherosclerosis and coronary heart disease (Ginsberg 1990).

there is a dose response relationship between the number of cigarettes smoked and cardiovascular morbidity and mortality (Wynder *et al* 1989).

Elevated total cholesterol protect effectively against coronary artery disease (Kerry& Robert 2007).

Smoking tend to increase blood total cholesterol levels and Aspartate transaminase(AST) activity in smokers compared to non smokers

(Narkiewiz 2005) the biological mechanism by which smoking or component of cigarette smoke influence bone loss are not well understood they may include local and systemic toxic effects on bone collagen synthesis alteration in metabolism of adrenal cortical and gonado hormone or other under mined mechanism(Krall & Dawson 1991).

1.2.Rationale

Cardiovascular disease complication associated with chronic hypercholesterolemia ,is found to be major health problem that is currently in increase.

Accelerated cardiovascular disease (coronary heart disease ,myocardial infarction)atherosclerosis including hypercholesterolemia ,obesity ,hypertriglyceridemia were report to be association to cigarette smoker

The enzymeAspartate transaminas (AST) activity it is found to biological marker which can be adversely at the smokers and this my leading to increase the risk of heart disease in cigarette smokers the for this is study was conducted to high light the risk of alteration of lipid(total cholesterol level and Aspartate transminase activity) in Sudanese cigarette smokers .

1.3 Objectives;-

1.3.1 General Objective:

To assessment of serum total cholesterol level and aspartate amintrasferase (AST) activity in cigarette smokers .

1.3.2 Specific Objectives:

1 -To assess of serum total cholesterol level and aspartate aminotrasferase (AST) activity in the blood of Sudanese may smokers with comparison Non cigarette smokers.

2 -To correlate the duration of smoking ,age of smokers and the number of cigarette smoked per day with serum total cholesterol level in cigarette smokers.

3-To correlate the duration of smoking ,age of smokers and the number of cigarette smoked per day and aspartate aminotrasferase (AST) activity in cigarette smokers.

CHAPTER TWO

Literature Review

2.Ch r two

2.1 Literature review

2.1.1 Structure of cigarettes

Cigarettes are a small roll of porous paper containing a rod of chopped up tobacco leaf. Cigarettes are designed so that the tobacco can be smoked, by lighting the cigarette and breathing in the smoke. At the mouth end of the cigarette there is a second layer of porous paper (called tipping paper) and a filter. The tipping paper is designed to allow fresh air to infiltrate when the smoker inhales. This fresh air reduces the harshness of the smoke. The filter cools the smoke and reduces the flow of smoke out of the cigarette.

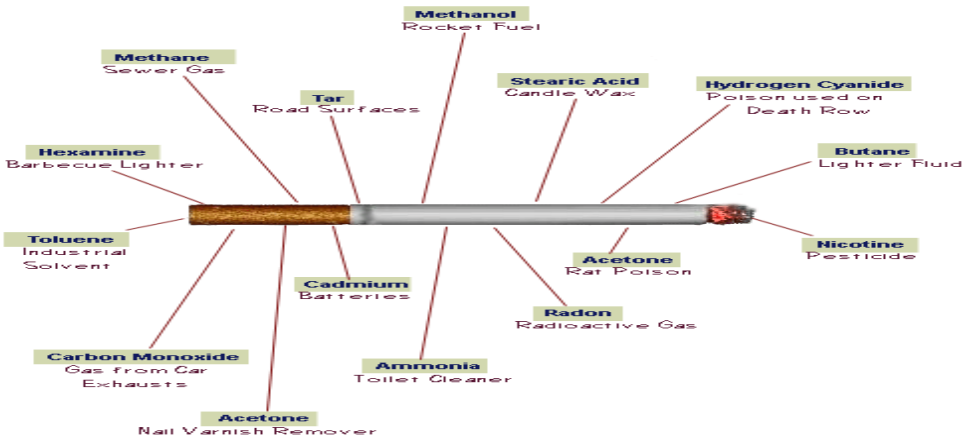
Cigarettes also contain additives such as sugars and flavourings which are used to increase shelf life, control the rate at which the cigarette burns and control the delivery of the chemicals.

Cigarettes vary in strength, taste and intensity depending upon:

The type of tobacco leaf that is used;

Where on the tobacco plant it is taken from;

The way the leaf is cured (Manecklee 1994)



Structure of cigarettes(Manecklee 1994)

2.1.2 Smoking tobacco;

Tobacco ,one of the most widely used addictive substance in the world ,is a plant native to the Americas and historically one of the half-dozen most important crops grown by Americas farmers. From 1617 to 1793 tobacco was the most valuable staple export from the English American mainland collies and the united states. Until the 1960s ,the united states not only grew but also manufactured and exported more tobacco than any other country .since 1964conclusive epidemiological evidence of the deadly effects of tobacco consumption has led to a sharp decline in official support for producers and manufacturers of tobacco ,in spite of its indisputably large contribution to the agricultural ,fiscal, manufacturing ,and exporting sectors of the economy.

Tobacco smoking is the act of burning the dried or cured leaves of the tobacco plant and inhaling the smoke for social (such as peer pressure or ritualistic)

purposes ,self –medication, or to satisfy addiction .the practice was common among native Americans throughout North and South Americas ,and was later introduced to the rest of the world ,via trade ,following European exploration of the Americas (Woo kc *etal* 1997).

Tobacco smoke contains nicotine ,an addictive stimulant. The effect of nicotine in first time or irregular users is an increase in alertness and memory ,and mild euphoria .in chronic users, nicotine simply relives the symptoms of nicotine withdrawal ;confusion ,restlessness, anxiety and insomnia withdrawal symptoms in chronic users begin to appear approximately 30 minutes after every dose .also disturbs metabolism and suppresses appetite (Manecklee 1994).

2.1.3 Chemicals components of cigarette:-

Chemical compounds found in all phases of cigarette smoke have been associated with independent negative effects on the smoker, which means they produce their own separate damage. These are just some of these chemicals found in cigarette smoke;

i.Nicotine:

Nicotine is harmful component of tobacco smoke, which cause an addiction to smoking its stimulate and increases activity in brain just like heroin ,caffeine and cocaine the effect of nicotine in the first time .acts as an agonist that attaches to nicotine acetylcholine receptor sites in the brain and body. Some of these neurons influence.

Containing is a byproduct of the metabolism of nicotine which remains in the blood for up to 48 hours.

Nicotine increase dopamine levels in the reward circuits of the brain

(Parkin *et al* 1998) When A cigarette is smoked .nicotine rich blood passes from the lungs to the brain within seven seconds and immediately stimulates the release of many chemical messengers (Robicsek 1979).

Chemical properties;

i. Nicotine easily penetrates the skin.
ii. Nicotine will burn at a temperature below its boiling point.
iii. Nicotine is a hygroscopic oily liquid that is miscible with water in its

Base from as a nitrogenous base

Nicotine from salts with acids that are usually solid and water

(Diereville *etal* 1993).

ii.Polycyclicaromatichydrocarbons.

These chemical names may not mean very much to most people until they realise where else these chemicals are found and then it becomes evident just how harmful they are. The following is a list of some chemicals found in cigarette smoke .

Is one component but is effect on a there thrombotic disease have been equivocal .an earlier study suggested that co could be responsible for smoking relate cardiovascular alterations however more result data suggest that Carbon monoxide from cigarette smoke was an unlike cause of atherosclerosis or thrombus((Diereville *etal* 1993).

iii.Tar

Tar is a mixture of the compounds in cigarette smoke which condensate (turn from a gas to a solid) once in the lungs to form a sticky brown substance, this is the cigarette smoke condensate. Tar is the part of cigarette smoke which causes the yellow-brown stains on teeth and fingers. Tar is made of nitrogen, oxygen, , carbon hydrogen, carbon dioxide monoxide, and a wide range other chemicals.

These chemicals have short and long term effects on health. The short term effects include coughing and shortness of breath (Lakatos *etal* 2007).

2.1.4 Method of smoking:

Various smoking equipment including different pips.

A.Pipe:

A pipe for smoking typically consists of a small chamber(bowl) for combustion of the substance to be smoked and thin stem(shank) that ends in mouth piece (also called a bit)Pipes are mode from a variety of materials briar, wood, glass, and various other materials.

Such as metal .tobacco used for smoking pipes is often chemically treated altered to change smell and taste not available in other tobacco products sold commercial (Heckewelder *etal* 1971).

B.Cigar;

A cigar is a cylinder of tobacco rolled in tobacco leaves for smoking they come in many shape and size (Robicsek 1979).

C.Hookah ; (sheesha)

A hookah or sheesha are sometime loaded with hashish or opium. In the Far East opium and cannabis are also among is type of traditional drug used .a pipe which operates by water –filtration and indirect heat.

Typically, tobacco is smoked from a hookah by placing exotic, richly flavored tobacco in the Smoking bowl, covering it with foil and placing a coal on top of the foil .this keeps the tobacco from Burning and allows it to back .the resulting vapors are further cooled by the hookah water However water is not effective for removing all relevant toxins e.g. The carcinogenic aromatic hydrocarbons are not water –soluble. Several serious negative health effects are linked to hookah smoking .that it is more harmful to health than cigarettes (Parrott & Winder 1989).

D.Kretek

Kretek are cigarettes made with a complex blend of tobacco, cloves and a flavoring "sauce". It was first introduced in the 1880s in Kudus, Java, to deliver the medicinal eugenol of cloves to the lungs. The quality and variety of tobacco play an important role in kretek production, from which kretek can contain more than 30 types of tobacco (Missmer *etal* 1991).

E.Electronic cigarette

Are an alternative to tobacco smoking, although no tobacco is consumed. It is a battery-powered device that provides inhaled doses of nicotine by delivering a vaporized propylene glycol/nicotine or vegetable glycerin/nicotine solution (Parkin *etal* 1998) .

F.Passive smoking;

Passive or involuntary smoking occurs when the exhaled and ambient smoke (otherwise known as environ mental or second hand smoke) from one persons cigarette is inhaled by other people (Parkin *etal* 1998).

Passive smoking involves inhaling carcinogens toxic components, that are present in second hand tobacco smoke include benzene, butanone, and many others (Robicsek 1979).

It is confirmed that in adults, exposure to second hand smoke causes lung cancer, nasal sinus cancer, and breast cancer in younger women, heart disease, and asthma induction (Schwartz & Marshall 1971).

2.1.5 Smoking prevalence;

I. About a third of the male adult global population smokes.

II. Smoking related –diseases kill one in 10 adults globally or cause four million deaths. By 2030 ,if current trends continue , smoking will kill one in six people

III. Every eight seconds , someone dies from tobacco use.

IV. Smoking is on the rise in the developing world but falling in developed nations .among Americans ,smoking rates shrunk by nearly half in three decades (from the mid-1960sto mid- 1990s) falling to 23% of adults by 1997 .in world ,tobacco consumption is rising by 3.4% per year (Langesen &Mend1991)

V. About 15 billion cigarettes are sold daily –or 10 million every minute.

VI. About 12 times mores British people have died from smoking than from world war .

VII. Cigarettes cause more than one in five American deaths (Peto -1994).

In 2005,24 per cent of adult aged 16 over in Great Britain smoked cigarettes ,indicating a slight fall in the prevalence of smoking among both men and women since the late 1990s .

The proportion of adults who smoked cigarettes fell substantially in the 1970s and early 1980s – from 45percent in 1974 to 35 per cent in 1982 after 1982 it declined gradually until the early 1990s .leveling out during the 1990s ,it then fell smoothly from 28 per cent in 1998/99 to 24 per cent in 2005 (Langesen 1994).

In July 2004 the British government set a new target to reduce the overall proportion of cigarette smokers in England from 28 per cent in 1996 to 21 per cent or fewer by 2010 –with a reduction from 32 to 26 per cent or less among manual occupation groups .in England in 2005 ,29 per cent of those in manual occupational groups were cigarette smokers ,compared with 33 per cent in 1998 .together with the fall in overall prevalence, this indicates some progress towards targets.

While men still more likely than women to smoke cigarettes the gap has narrowed ,in 1974 ,51 per cent of men and 41 per cent of women smoked .in 2005,25 per cent of men and23 per cent of women were cigarette smokers (Langesen 1994).

cigarette smoking contines to be more common among adult aged 20 to 34 than among other age groups .in 2005,32 per cent of adult aged 20 to 24 and 31 per cent of adult aged 25 to 34 were smokers compared with 14 per cent of those aged 60 and over (Cupta *etal* 1992).

the proportion of men who were heavy smokers (on average 20 or more cigarettes a day) fell from 14 per cent in 1990 to 10 per cent in 1998 among women the proportion fell from 9 per cent to 7 per cent over the same period. Since then the proportions have remained virtually unchanged , although there is a suggestion of a slight downturn in the last couple of years. the proportion of adult smoking fewer than 20 cigarettes a day has been around 17 to 19 per cent of both men and women since 1998 (Peto 1994).

In 2005just over two thirds (68 per cent) of cigarette smokers in Great Britain said that they wanted to give up .but 56 per cent said it would be difficult to go without smoking for a whole day . overall 16 per cent of smokers said they had their cigarette of day within five minutes of waking up ;this varied according to how much respondents smoked ,ranging from only 2 per cent of those who smoked fewer than 10 a day to 33 per cent of those who smoked 20 or more cigarettes a day (Peto 1994).

Table;(2.1)

Estimated number of smokers in the world (early 1990s in million)

(Cupta *etal* 1992).

Countries	**Male**	**Female**	**Total**
Developed countries	200	100	300
Developing countries	700	100	800
World	900	200	1100

Table ;(2.2)

Estimated smoking prevalence for men and women, 15 years of age and over of population by WHO region early 1990s (Peto 1994).

Who region or countries	**Men(%)**	**Women(%)**
African region	29	4
Region of Americas	35	22
Eastern Mediterranean region	35	4
European region	46	26
south-east Asia region	44	4
Western pacific region	60	8
More developed countries	42	24
less developed countries	48	7
World	47	12

2.1.6 Disease caused with smoking ;

Smoking harms nearly every organ of the body .causing many diseases, and reduces quality of life and life expectancy .it has been estimated that .in England ,364.000 patients are admitted to hospitals each year due to diseases caused by smoking .this translates in to 7.000 hospital admission per week,or1.000 day .for every death caused by smoking approximately 20 smokers are suffering from a smoking related disease (Benouwitz 1998). Half of all teenagers who are currently smoking will die from diseases caused by tobacco if they continue to smoke .one quarter will die after 79 years of age and one quarter before ,with those dying before 7o losing on average 21 years of life .it is estimated that between 1950 and 2000 six million .60 million people worldwide .died from tobacco –related diseases (Benouwitz 1998).

Smokers face higher risk than non –smokers for a wide variety of illnesses ,many of which may be fatal .however. many ,medical conditions associated with smoking while they may not be fatal ,may cause years of debilitating illness or other problems (Mortality statistics 2005).

These are included in the coming tables;

Table;(2.3)

Disease risk increased by smoking (Mortality statistics 2005).

Acute necrotizing ulcerative gingivitis (gum disease)	Muscle injuries
Angina (20 x risk)	Neck pain
Back pain	Nystagmus (abnormal eye movements)
Burgers' disease(severe circulatory disease)	Ocular histoplasmosis(fungal eye infection)
Duodenal ulcer	Osteoporosis(in both sexes)
Cataract(2 x risk)	Osteoarthritis
Cataract ,posterior sub capsular (3 x risk)	Penis(erectile dysfunction)
Colon polyps	Peripheral vascular disease
Crohns disease(chronic inflamed bowel)	Pneumonia
Depression	Psoriasis (2 x risk)
Diabetes (type 2 ,non –insulin dependent)	Skin wrinkling(2 x risk)
Hearing loss	Stomach ulcer
Influenza	Rheumatoid arthritis (for heavy smokers)
Impotence(2 x risk)	Tendon injuries
Optic neuropathy (loss of vision,(16 x risk)	Tobacco Amblyopia (loss of vision)
Ligament injuries	Tooth loss

Table;(2.4)

Function impair and symptoms worse in smoker (Calhaz 2004).

Ejaculation (volume reduced)	Sperm count reduced
Fertility (30% lower in women)	Sperm motility impaired
Immune system(impaired)	Sperm less able to penetrate the ovum
Asthma	Graves disease (over-active thyroid gland)
Chronic rhinitis (chronic inflammation of the nose)	Multiple sclerosis
Diabetic retinopathy(eye)	Optic neuritis (eye)
Menopause (onset 1.74 years early on average)	Sperm shape abnormalities increased

2.1.7 Cardiovascular diseases ;

Heart disease or cardiovascular disease is the class of diseases, that involve the heart or blood vessels,while the term technically refers to any disease that affects Cardiovascular system (Maton *etal*1993)Cardiovascular diseases

(CVD) is major cause of morbidity and mortality in the industrialized world (CVD) morbidity and mortality have increase dramatically over the last 30 years. an estimated 60 million Americans have some form of CVD, and approximately 1.5milion myocardial infarctions and 600.000 strokes occur every year CVD could be characterized as a disturbance in hydraulic (homodynamic) and /or electrical(electro physiologic) function. Coronary atherosclerosis (i.e vascular obstruction) has been designated as the ‘’prime mover’’ of cardiovascular disorders ,such that a series of atherogenic risk factors s were sought, and many were identified (e.g hypercholestoleamia , hypertension diabetes, obesity). Both our understanding of the etiology of CVD and our ability to manage the epidemic are still limit. For example, the Framingham heart study used epidemiologic techniques to identify important risk factors (smoking, diabetes ,hypertension, and cholesterol) however, these traditional risk factors explained only part of risk for CHD .in practical terms, this means that these standard risk factors fail to predict many of the new CHD cases .one of these factors essential hypertension is of practically unknown etiology (De Faire 1997) .

- **Path physiology of Cardiovascular diseases ;**

Obesity and diabetes mellitus are often linked to Cardiovascular diseases .in fact Cardiovascular diseases In most life threatening of the diabetic complications and diabetics are to four fold more likely to die of Cardiovascular related causes than non diabetics (Ridker 2003) .

Cardiovascular diseases(CVD) is the number one killer adults in the united states .Diabetes mellitus and CVD share several important characteristics .the incidence of both conditions increase with age :both are associated with an adverse lipid profile, obesity and a sedentary lifestyle .Diabetes is also a

potent independent risk factor for CVD cross-section epidemiologic studies have consistently shown an association between diabetes and prevalence of CVD (Braunwald 1997).

2.1.8. Types of heart diseases ;

Heart diseases may be acute or chronic .Acute heart disease used to describe a person who has suffered a heart attack (acute myocardial infarction)or chest pain due to an inadequate blood supply to the heart muscle (acute myocardial ischemia)that results from coronary heart disease Acute heart disease Can progress gradually over time as plaque(fatty deposits) builds in the arteries of the heart .plaque makes in hard for blood to flow freely through the arteries men who are over age 45and women older than 55 are more to suffer from acute coronary syndrome (Kannel *etal* 1976).

The most risk factors include high blood pressure ,high blood cholesterol,type2 diabetes, cigarette smoking. inadequate exercise and a family history of heart problems. the warning signs of acute coronary syndrome are often similar to those of a heart attack .symptoms include a burning chest (angina) that continues for several minutes .chronic heart disease is the primarily caused by myocarditis, heart dilatation and heart valve problems. chronic heart disease ,the number one killer in the United States ,is responsible for more than 40 percent of all deaths many cases of chronic diseases are caused by toxic scars. chronic heart disease can cause narrowed or blocked blood vessels and congestive heart failure

(Kannel *etal* 1976).

2.1.8.1 Ischemic heart disease (IHD)

IHD is single largest cause of death in the developed countries, and is one of the main contributors to the disease burden in developed countries .the two leading manifestations of IHD are angina and acute myocardial infarction .Angina is the characteristic pain of IHD.it is caused by atherosclerosis leading to stenosis (partial occlusion) of one or more coronary artaries .patients with chronic stable angina have an average annual mortality of 2 percent or less . acute myocardial infarction(AMI) is the total occlusion of a major coronary artery , with a complete lack of oxygen and nutrients lead to cardiac muscle necrosis (Kvan 2007).

2.1.8.2 stroke

Stroke is caused by a disruption in the flow of blood to part of the brain, either because of the occlusion of blood vessel (ischemic stroke) or the rupure of blood vessel(hemorrhagic stroke) many of the same risk factor for IHD apply to stroke in addition ,atrial fibrillation is an important risk factor for stroke .the annual risk of risk of stroke in patients with non valvular atrial fibrillation is 3 to5 percent with 50 percent of thromboembolic stroke being attributable to a trial fibrillation (Norhammar *etal* 2004)

2.1.8.3.congestive Heart failure (CHF)

CHF is the end stage of many heart diseases .it is characterized by abnormalities in myocardial function, and neurohormonal regulation resulting in fatigue ,fluid retention ,and reduced longevity .CHF is caused by pathological processes that affect the heart: IHD and hypertension- related heart disease are the most common etiologies. The risk of developing CHF is two times more in hypertensive men and three times more in hypertensive CHF is five times more common in those who have had an AMI than in those

who have not. The prognosis for those with established CHF is generally poor and worse than for those with most malignancies (DECODE 1999).

2.1.8.4. Rheumatic Heart Disease(RHD)

RHD is the consequence of an acute rheumatic fever (ARF) that is a poorly the adapted autoimmune response to group A Beta hemolytic streptococci it affects the connective tissue ,mainly the joints and the heart valves.the most serious complications are valvular stenosis ,regurgitation following the volvulitis ,or both.RHD is also apredisposing factor for infective endocarditis ,a disease of younger adults, predominantly males (Musaigre 2002).

According to 2001 estimates, RHD accounts for 33.000 deaths per year world wide,two-thieds of them in southeast Asia and the western pacific. About 12 million people in developing countries, most of them children,suffer from RHD (Antman 2004).

2.1.9 Risk Factors of cardiovascular diseases;

The risk of developing CVD depends to a large extent on the presence of several risk factors .the major risk factors for CVD include tobacco use ,high blood pressure,high blood glucose,lipid abnormalities. Obesity ,and physical inactivity .the global variation in these known risk factors, such as age ethnicity ,and dender .obviously cannot be modified ,most of the risk is attributable to lifestyle and behavioral patterns ,which can be changed (Wolf 1991).

2.1.9.1.Respiratory problems;

Respiratory problems can include increased coughing, phlegm, wheezing , chest colds and shortness of breath ,even in smoke as little as one cigarette a week (Berliner *etal* 1991).

2.1.9.2.Gastrointestinal Effects;

Peptic ulcer disease is more likely to occur in smokers than in non –smokers, when ulcers are present they heal less rapidly in smokers and are more likely to recur.

Evidence is accumulating that smoking is a risk factor for the occurrence of chronic bowel disease (crohns disease).as well , smoking may contribute to the recurrence of this disease (Hippe *etal* 1997).

2.1.9.3.Effects on teeth and gums;

Tobacco use is an important factor in oral health , apart from its role in causing oral cancer. smoking has also been linked to periodontal disease in younger people (Hippe *etal* 1997).

2.1.9.4.Effects in pregnancy;

Smoking is known to have an effect on babies before they are born .has a direct effect on the growth of the fetus. The more the mother smokes during pregnancy ,the lower the weight of the newborn infant. Smoking mothers give birth to infants who can weigh about 150grams less than a term than non- smokaers. Such babies.called “low birth weight “ babies are more likely to suffer adverse outcomes including stillbirth, the need for special treatment in neonatal intensive care units and death in infancy (Krishna *et al* 1991).

During pregnancy ,smokers have a greater risk of miscarriages and during the brith they are more likely to have complications .the chances of a baby dying at birth or shortly thereafter are increased if the mother has smoked during pregnancy.

More than 18% of all deaths from sudden infant death syndrome are due to maternal tobacco use .

Nursing mothers can pass along harmful chemicals from cigarettes to their babies in breast milk (Krishna *et al* 1991).

2.1.9.5 Bronchial carcinoma;

Bronchial carcinoma accounts for more than 50%of all male deaths from malignant disease it is more common in men than women and occurs most frequent between the ages of 50 and 75.

Cigarette smoking is responsible for most cases of bronchial carcinoma and directly increased risk is directly proportional to amount smoked and to the tar content of the cigarette.

For example the death rate from the disease in heavy cigarette smokers is 40 times that in non smokers (Heckeweelder *etal* 1971).

A. Clinical features:

i. Cough
ii. Chest pain
iii. Chest infection
iv. Weight loss
v. Malaise (Parveen&Michael 1994).

B. **Investigation**:

A-Radiological examination

B-Cytological examination

C-Tran bronchial lung biopsy (Toyce 1987).

C.Treatment:

Surgical treatment is practicable the average period of survival after diagnosis is less than a year (Toyce 1987).

2.2 Plasma lipid

The major lipid present in plasma is fatty acid

Triglyceride &cholesterol and phospholipids other lipid

(Marshall &Benger 1994).

2.2.1.Fatty Acids

Are straight chain carbon compounds the major lipid present in plasma are fatty acid of varying lengths they may be saturated containing no double bonds Monounsaturated with one or polyunsaturated with more than one

(Phili 1994).

Fatty acids are variable in length and can be classified as short –chain

(4-6 carbon atoms) medium-chain (8-12carbonatom)or long–chain

(.>12 carbon atoms) most fatty acid in our diet are of the long-chain variety and contain an even number of carbon atoms (Bishop &Schoeff 2000) .

may be esterified with glycerol to form Triglycerides, or be non esterified or free (NEFA or FFA).plasma FFA liberated from adipose tissue are transported, mainly bound to albumin to the liver and muscle where they are metabolized. They provide a significant proportion of the energy requirements of the body (Phili 1994).

2.2.2 Triglyceride

Are fatty acid esters of glycerol each containing three different fatty acid (Phili 1994).Molecules attach to one molecule of glycerol by ester bonds .because of the large number of possible forms fatty acids each fatty acid in the triglyceride molecule can potentially be different in structure producing many possible structural forms of Triglyceride (Bishop &Schoeff 2000).

they are transported fromThe intestine and the liver to various tissues, such as adipose tissue, as lipoproteins, following hydrolysis, fatty acids are taken up,

re esterified and stored as Triglyceride .plasma Triglyceride concentrations rise after a fatty meal and remain increased for several hours.

(Bishop &Schoeff 2000).

2.2.3Cholesterol

steroid of unsaturated alcohol with high molecular consists of no polar rings, so is completely insoluble in water.

is an unsaturated steroid alcohol containing 4 rings (A-B-C and D) and single C-H chain tail a(Bishop &Schoeff 2000) steroid ,is a precursor to many physiologically important steroids, such as bile acids and steroid hormones (Phili 1994)Cholesterol is required to build and maintain membranes it modulates membranes fluidity over the range of physiological temperatures (Koren *etal* 1991) .

2.2.4 Phospholipids

Phospholipids is similar in structure to triglyceride but containing phosphate and nitrogenous base in place of the fatty acid they are important of cell membranes and lipoproteins maintaining the solubility of non polar lipids and cholesterol the most common phospholipids found on lipoproteins and in cell membranes the two fatty acids in phospholipids are normally14-24carbon atoms long,with one fatty acid commonly saturated and the other un saturated .because phospholipids contain both hydrophobic fatty acid C-H chains and a hydrophilic head group found Elevated plasma concentration of lipid

(Bishop &Schoeff 2000)particularly cholesterol are causally related to pathogenesis of atherosclerosis the process responsible for the majority of cardiovascular disease cerebrovascular and peripheral vascular disease is the common cause of death (Marshall 2004).

2.3Function of lipid

1-Important of lipid in biological process:

2-Energy source (carbohydrate-lipids)

3-energy storage (most stored in body in the from lipid)

4-cell membrane structural component (phosphoglycerid-sphingolipid)

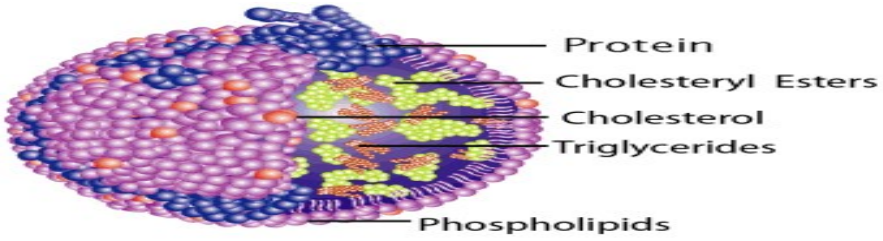
5-Hormone steroid hormone are chemical messenger that allow tissue of the body

6-vitamin a absorption dietary fat serves as carrier lipid soluble vitamin (Katherine 2001).

2.3.1 Lipoproteins

2.3.1.1 Strurure of Lipoproteins;

Lipoprotein particles range in size from 10 to 1000 nanometers. The largest lipoproteins are about one tenth the size of a red blood cell. The density of lipoproteins increases in proportion to their ratio of proteins to lipids. In general, as the density of a lipoproteins increases, the size of the particles decreases. The outer layer of a lipoprotein consists of a water-soluble (hydrophilic) layer of apolipoproteins, phospholipids and cholesterol. The center of a lipoprotein is composed of cholesteryl esters, triglycerides, fatty acids and fat-soluble vitamins like Vitamin E (Allain *etal*1974).



Strurure of Lipoproteins(Allain *etal*1974).

2.3.1.2 Classification of lipoproteins

Triglycerides rich particles include;

A.Chylomicrons; which transport exogenous lipid from the intestine to al cell.

B.Very low density lipoproteins (VLDL);which transport endogenous lipid from the liver to cell.

C.intermediate density lipoproteins (IDL) ; which are usually undectable in normal plasma ,it is normally a transient intermediate lipoprotein formed during the conversion of VLDL to LDL.

Because of tier large size ,these particles reflect light and plasma containing high concentration appears turbid or milkly (lipaemia) , if turbid plasma sample is left standing for 18 hours at 4 c^{o} the larger chylomicrons. because of their low density , rise to form a creamy layer on the surface .the smaller .denser VLDL and IDL particles do not rise and the sample remains diffusely turbid (Whitby *et al* 1987).

Cholesterol rich particles;

A.Low density lipoproteins(LDL);formed from VLDL , transport cholesterol to cells.

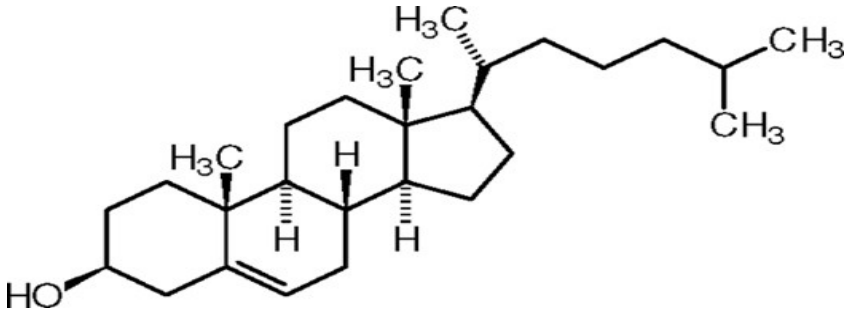
B.High density lipoproteins (HDL);are involved in the transport of cholesterol from the peripheral Lp(a) is similar in composition to LDL but has a higher protein content , it contains a protein which is structurally similar to the clotting factors .it is synthesized in the liver and normally present in low plasma concentrations (Whitby *etal* 1987).

Classification of lipoproteins(Whitby *etal* 1987).

2.4.Cholesterol

2.4.1 Structure of cholesterol

White crystalline substance, $C_{27}H_{45}OH$, found in various foods, that is normally synthesized by the liver Cholesterol is only slightly soluble in water; it can dissolve and travel in the water-based bloodstream at exceedingly small concentrations.



2.4.2 Function of cholesterol

Cholesterol is essential constituent of cell membrane Cholesterol is required to build and maintain membranes it is also precursor of bile acid including vitamin D a cell can either synthesize cholesterol or acquire it from it environment cell can also acquired cholesterol from outside the cell through Plasma membrane low density lipoprotein LDL receptor which mediate lipoprotein internalization in to the cell satisfied it need for cholesterol by balance between synthesis and import)Dominiczak 1999) .

cholesterol is the precursor molecule in several biochemical pathways. In the liver, cholesterol is converted to bile, which is then stored in the gallbladder Cholesterol is required to build and maintain in intracellular transport, cell. Cholesterol is essential for the structure Cholesterol is an important precursor molecule the steroid hormones including the adrenal gland hormones cortisol

and aldosterone as well as the sex hormones progesterone, estrogens, and testosterone, and their derivatives (Koren *etal* 1991).

2.4.3 Source of cholesterol:

Either endogenous (body) or exogenous(diet).diet contribute about 100-700 mg/day of cholesterol ,a bout 500-1000 mg/day synthesized in the liver and other tissue, about 600-1000 mg/day excreted from bilialary tract about 50% of which can be reabsorbed in to the blood through liver 74% located into skin .adipose tissue, intestine and muscle cell (stationary pool)the remain portion (mobile pool) bound to protein mainly albumin in from of lipoprotein and transported through blood esterified with fatty acid to form ester cholesterol.1/3present as free cholesterol (Bishop *etal* 2006).

2.4.4.Synthesis of cholesterol

The liver is the major site of cholesterol synthesis, although cholesterol is also produced in many other organ and tissues (Bishop *etal* 2006).

Focusing on the enzyme the regulated sterol intermediates and the location of enzymes in the cell sterol are synthesized from the two carbon building black acetyl CoA the soluble enzyme ace to acetyl CoA thiolase interconvert acetyl CoA and ace to acetyl CoA which are then condensed by 3-hydroxy -3methyl glatryl (HMG) –CoA syntheses to from HMG –CoA there are two form of HMG-CoA syntheses mitochondrial form involved in cytogenesis predominate in the liver (Vance 2002).

HMG reductases catalyzes the reduction of HMG CoA to mevalonte

HMG CoA reductases mevalonic acid is converted into squalene after series of converted into squalene modified to yield cholesterol .the Synthesis of cholesterol in the liver regulated by the intracellular cholesterol concentration

and activity of HMGCO reductase rate determinately enzyme of cholesterol biosynthetic pathway (Vance 2002).

Hormonal effects cholesterol biosynthesis:

Insulin stimulates HMG.COA reducates activity.

Glucagon antagonizes the effect of insulin.

Thyroid hormone HMG.COA reducates activity

The drug levitation whaich is used to treat hypercholesterolemia blocks endogenous cholesterol synthesis by inhibiting HMG.COA reeducat (Davidson.& Sittman 1999).

2.4.5.Cholesterol absorption

The average diet estimated to contain approximately 300 to 450 mg of cholesterol per day which mostly comes from the consumption of human A similar amount of cholesterol enters the gut from billiard secretion and the turnover and release intestine (Ash wood 2001).

In order to be absorbed cholesterol is solubilied by formation of mixed micelles containing unsterilized cholesterol fatty acid monoglyceried phospholipids and conjugate bile acid these micelle also facilitate cholesterol transport across the luminal cell traffics in absence bile acids (Tietz 1976) .

Digestion and absorport of both cholesterol and triglycerides are severely impaired on the average 30- 60% dietary and intestinal cholesterol is absorbed daily to maximum of 1g/day when the oral intake reaches 3g/day (Tietz 1976).

2.4.6.Transportation of cholesterol

Cholesterol consists of no polar rings, so is completely insoluble in water. Therefore it has to be transported in lipoproteins as either bile salts or

cholesteryl esters. There are different densities of lipoproteins high density (HDL) and low density (LDL) is sometimes known as "bad" cholesterol and is responsible for transporting cholesterol form the liver. HDL is known as "good" cholesterol is transported in the watery fluids of the body in lipoproteins. These carriers are water soluble on the outside and fat soluble onthe inside. The Water soluble coating allows cholesterol and other fats to move throughout the body without clogging blood vessels and other tissues (Vila *etal* 2004).

The food fed on the cholesterol and triglycerides, after absorption from the intestine of the Chylomikronen and then transported into the tissue. Different density lipoproteins (VLDL, IDL and LDL) carry themselves recorded and produced cholesterol from the liver to the tissues. HDL cholesterol takes from the tissues and brings it back to the liver. The cholesterol in lipoproteins is predominantly esterifies with fatty acids. The range of these fatty acids is strongly influenced by the food (Koren *etal* 1991).

2.4.7.Normal Rang of cholesterol:

Cholesterol concentration at birth below 2.5mmol/l (100mg/dl) increase slowly but not exceed than 4.0 mmol/l (160 mg/dl) in children in adult 5.2 mmol/l (200 mg/dl) more in men than women during reproductive years (affected by age and sex) (Phili 1994.).

Cholesterol as predictor of cardiovascular diseases

Cholesterol is novel and traditional biochemical risk markers ,of ischemic heart disease morbidity ,and mortality in both diabetics and non –diabetics. Besides total cholesterol ,elevated triglycerides high LDL Cholesterol have also been shown to independently increase cardiovascular mortality in diabetics patients .

Recently prospective studies illustrated that many cases of cardiovascular diseases like stroke ,ischemic heart disease and myocardial infarction, occur with normal level of cholesterol ,which create the need of anew sensitive predicator for cardiovascular diseases (William *etal* 1998)

2.5 Plasma lipids and cardiovascular disease;

Plasma cholesterol concentration is correlated with the incidence of ischemic heart disease. But not necessarily as cause and effect. There is noclear cut – off between normal values and increased risk , however it appear to be a particularly high risk ,with a rapidly rising incidence.of ischemic heart disease if plasma total cholesterol exceeds 6.0 mmoL/L(235mg/dl).

Thre is a positive correlation between the risk of developing ischemic heart disease and raised plasma total and LDL –cholesterol concentration and a negative one with plasma raised HDL-cholesterol concentration.

Lowering high plasma LDL-cholesterol concentration reduce the risk of cardiovascular disease. Hypercholesterolemia ,is just one of the major risk factor of cardiovascular disease .other include smoking and hypertenstion (Stryer 1998).

2.5 .1 Hypercholesterolaemia

2.5.1. 1. Primary Hypercholesterolaemia

The familial incidence of Hypercholesterolaemia ,often associated with an increased risk of ischemic heart disease .men adult level of total cholesterol (TC) vary in different communities throughout the world from about 3.9 mmoL/L(150 mg/dl) to over7 mmoL/L(275 mg/dl). When community levels are compared with IHD mortality rates , a strinking corris observed .the international atherosclerosis project ,which investigated autopsy material from over 20.000 individuals in various cities through out the world

,demonstrated also a strong association between the mean total cholesterol levels for various communities and the prevailing serverity of atheroma (Murray *etal* 1999) .

Primary hypercholesterolaemia is transmitted by an autosomal dominat inheritance.

Homozygoute commonly develop flat cutaneous and tendon xanthomas ,and usually die from ischemic heart disease in early adult life.

In heterozygote the number of LDL receptors is reduced by about 50 percent and the plasma concentrations are about twice these in normal subject . they have a 10 to 20 fold higher risk of developing ischemic heart disease than those with normal plasma concentration (Murray *etal* 1999) .

2.5.1.2 Secondary hypercholesterolaemia;

The commonest disorders that may produce a secondary increase in plasma total cholesterol concentration are;

i. Primary Hypothyroidism
ii. Nephritic syndrome
iii. Chronic renal failure
iv. Cholestasis
v. Diabetes mellitus
vi. Some drugs (Whitby 1987).

These disorders must be excluded in any patient presenting with hypercholesterolemia.

2.5.3.Treatment of Hypercholesterolemia

A.Nicotinic acid: Nicotinic acid reduces the plasma levels of both VLDLs and LDLs by inhibiting hepatic VLDL secretion, as well as suppressing the

flux of FFA release from adipose tissue by inhibiting lipolysis. In addition, nicotinic administration strongly increases the circulating levels of HDLs.

B.Cholestyramine or colestipol (resins): These compounds are non absorbable resins that bind bile acids which are then not reabsorbed by the liver but excreted. The drop in hepatic reabsorption of bile acids releases a feedback inhibitory mechanism that had been inhibiting bile acid synthesis.

C.Ezetimibe functions to reduce intestinal absorption of cholesterol, thus effecting a reduction in circulating cholesterol. The drug functions by inhibiting the intestinal brush border transporter involved in absorption of cholesterol (Bucoio &David 1973).

2.5.2. Hypertriglyceridaemia;

Elevated plasma triglyceride concentration may be due to increase in plasma VLDL or chylomicrons or both . Hypertriglyceridaemia is usually secondary to another disorder , primary Hypertriglyceridaemia is less common than primary hypercholesterolemia.

2.5.3. Causes of secondary Hypertriglyceridaemia;

a. obesity and excessive carbohydrate intake
b. Primary hypothyroidism
c. Alcohol
d. Nephritic syndrome
e. Chronic renal failure
f. Cholestasis
g. Diabetes mellitus
h. Some drugs (Whitby 1987)

2.6. Atheroma (Atherosclerosis);

In most developed countries this is responsible for more deaths than any other disease .it causes narrowing of the lumen of arteries ,and it is the major causes of disability and death from heart disease ,cerebral infraction and ischaemia of the lower limbs, due mainly to accumulation of lipids , proliferation of smooth muscle cells and formation of fibrous tissue (Anderson 1988).

The considering further the importance of plasma lipid ,it may be recalled that about 70 %off cholesterol is carried low density lipoproteins(LDL), about 20 % in the high density lipoproteins and only a small percentage in very low density lipoproteins(VLDL).the level of LDL relater closely to total cholesterol (TC) levels , and prospective studies which have included lipoprotein assays have demonstrated that LDL levels are predictive of the risk of IHD .plasma levels of HDL are related inversely to the risk of IHD (Murray *eta*l 1999).

2.7 Relationship between smoking and lipid :

Smoking is a major cause of atherosclerosis — a buildup of fatty substances in the arteries. Atherosclerosis occurs when the normal lining of the arteries deteriorates, the walls of the arteries thicken and deposits of fat and plaque block the flow of blood through the arteries. In coronary artery disease, the arteries that supply blood to the heart become severely narrowed, decreasing the supply of oxygen-rich blood to the heart, especially during times of increased activity. Extra strain on the heart may result in chest pain (angina pectoris) and other symptoms. When one or more of the coronary arteries are completely blocked, a heart attack (injury to the heart muscle) may occur.
In peripheral artery disease, atherosclerosis affects the arteries that carry blood to the arms and legs. As a result, the patient may experience painful

cramping of the leg muscles when walking (a condition called intermittent claudicating) Peripheral artery disease also increases the risk of stroke (Bottcher & Falk 1999).

2.8 Aspartate transaminase (AST):

Aspartate transaminase (AST), also called aspartate aminotransferase (AspAT/ASAT/AAT) or serum glutamic oxaloacetic transaminase (SGOT), is a pyridoxal phosphate (PLP)-dependent transaminase enzyme (EC 2.6.1.1). AST catalyzes the reversible transfer of an α-amino group between aspartate and glutamate and, as such, is an important enzyme in amino acid metabolism. AST is found in the liver, heart, skeletal muscle, kidneys, brain, and red blood cells (Kirsch *etal* 1984).

2.8.1 Function ;

Aspartate transaminase catalyzes the interconversion of aspartate and α-ketoglutarate to oxaloacetate and glutamate.

Aspartate (Asp) + α-ketoglutarate ↔ oxaloacetate + glutamate (Glu)

Reaction catalyzed by aspartate aminotransferase

As a prototypical transaminase, AST relies on PLP as a cofactor to transfer the amino group from aspartate or glutamate to the corresponding ketoacid. In the process, the cofactor shuttles between PLP and the pyridoxamine phosphate (PMP) form(Kirsch *etal*1984) The amino group transfer catalyzed by this enzyme is crucial in both amino acid degradation and biosynthesis. In amino acid degradation, following the conversion of α-ketoglutarate to glutamate, glutamate subsequently undergoes oxidative deamination to form ammonium ions, which are excreted as urea. In the reverse reaction, aspartate

may be synthesized from oxaloacetate, which is a key intermediate in the citric acid cycle (Berg 2006).

2.8.2 Isoezyme;

Two isoenzymes are present in a wide variety of eukaryotes. In humans:

1.GOT1/cAST, the cytosolic isoenzyme derives mainly from red blood cells and heart.

2.GOT2/mAST, the mitochondrial isoenzyme is present predominantly in liver.

These isoenzymes are thought to have evolved from a common ancestral AST via gene duplication, and they share a sequence homology of approximately 45%. (Hayashi *etal* 1990).

2.8.3 Clinical significance ;

AST is found in the liver, heart (cardiac muscle), skeletal muscle, kidneys, brain, and red blood cells (Goldberg &Kirsch 1996).

AST may be elevated also in diseases affecting other organs, such as

1-myocardial infarction.

2- acute pancreatitis.

3-acute hemolytic anemia.

4-severe burns.

5-acute renal disease.

6-musculoskeletal diseases.

7-trauma (Gaze DC 2007).

AST was defined as a biochemical marker for the diagnosis of acute myocardial infarction in 1954. However, the use of AST for such a diagnosis is now redundant and has been superseded by the cardiac troponins

AST (SGOT) is commonly measured clinically as a part of diagnostic liver function tests, to determine liver health. .(Gaze DC 2007).

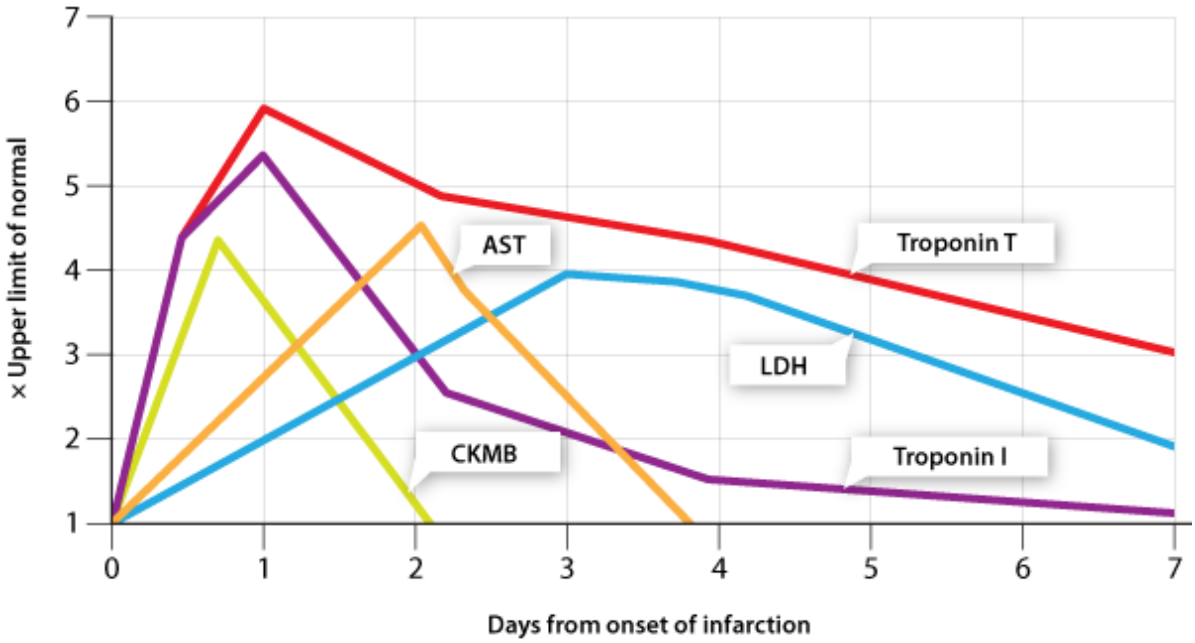


Figure (2.1) correlation between cardiac enzyme& days from onset of infarction.

CHAPTER THREE

Materials and methods

3. Chapter three

3.1 Materials and Methods

3.1.1 Materials:

3.1.1.1 Study approach

A quantitative methods were used to measure total cholesterol level and aspartate transminase(AST) activity in Sudanese with cigarette smokers in Khartoum state ,during the period from May to September 2013 .

3.1.1.2 Study design

Cross-sectional , case control.

3.1.1.3 Study area

Khartoum state .

3.1.1.4 Study population

The test groups compare 50 with cigarette smokers and 50 non cigarette smokers as control group.

3.1.1.5 Inclusion criteria

Sudanese with cigarette smokers .

3.1.1.6 Exclusion criteria

The Exclusion criteria non cigarette smokers ,alcohol intake ,hypertensive and cardiac diseases.

3.1.1.7 Study variables

Serum total cholesterol level was measured colometer method.aspartate transaminase(AST) activity enzyme was measured by spectrophotomerically .age of subjects ,duration, and number of cigarette smokers per day .

3.1.1.8 Sampling

Non –probability sampling technique was carried out.

3.1.1.9 Sampling frame

Cigarette smokers writhing Khartoum state .

3.1.1.10 Sampling unit

The study was restricted to males with cigarette smokers.

3.1.1.11 Sampling size

Fifty cigarette smokers as the test group and 50 normal healthy non smokers as a control group were selected.

3.1.1.12 Data collection method and tools

Data were collected by using a structural interviewing questionnaire ,which is designed collect and maintain all valuable information concerned each case examined.

3.1.1.13 Sample collection and processing:

Blood sample (2.5ml) was collected from each smokers and non smokers as well as control .All centrifuged at 400 rpm to obtain the serum. 10µl serum was obtained without Hemolysis form total cholesterol level and 100µl serum obtained from Aspartate transaminase(AST)activity.

3.2.1. Methodology:

3.2.1.1 Determination of cholesterol:

3.2.1.2 Principle

Cholesterol esterase(CHO)catalyses the hydrolysis of cholesterol esters to produce cholesterol which is oxidized by cholesterol oxidase (CHO) to yield hydrogen peroxide (H2O2) .in coupled reaction catalyzed by peroxidase(POD) quinoneimine dye (red) is formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidae. The

absorbance of the dye at 520 nm is proportional to the concentration of cholesterol in the sample (Allain *etal* 1989).

3.2.1.3 Requirement:

- Colorimeter
- Centrifuge
- Automatic pipette
- Sterile needle
- 70% alcohol
- Cotton
- Constant temperature
- Cuvette
- Test tubes

3.2.1.4 Reagent preparation and stability

The reagent and stander are provided ready to use and are stable up to the expiry date when sealed and store at

2-8 OC

3.2.1.5Technique;

The reagent were first brought to room temperature, then the following amounts were pipette according to the table below

	Blank	standard	Sample
Reagent	1.0 ml	1.0 ml	1.0 ml
Cholesterol standard(s)	-	10 µl	
Sample (serum)	-	-	10 µl

- mix and incubate the tubes for 10 minute at room temperature.

.Measure the absorbance (A) of the standard and sample were measured at 520 nm against the blank

3.2.1.6 Calculation:-

$\frac{A\ Sample}{}$ X C standard = C sample mg/dl

A standard

C= concentration

3.2.1.7 Normal values of cholesterol :

At birth	up to	100 mg/dl
Children	up to	160 mg/dl
Adult	up to	200 mg/dl.

3.3. Determination of Aspartate transaminase:

3.3.1 Principle :

Aspartate transaminase catalyzes the transfer of amino group ($NH_{2)}$ from aspartate and α-ketoglutarate to oxaloacetate and glutamate. In alkaline PH during with formed reverisible reaction with the for mation of glutamate andoxaloacetate with theyreduced in to malate by malate hydrogenase in alkaline PH in present of their its reduced form of NAD (NADH).the catalytic rate of reaction in monited kinetically at 340 nm by decease rate in absorbance reducing increase oxidation NADH in to NAD+ and direct proportion aspartate aminotransferase with in sample (Henry1960).

3.3.2 Procedure;

-pre incubated work reagent .sample and control to reactioaan temperature 37c^{o} -set the photometer to absorbance with distilledwater .

-pipette in to acuvette .

- working reagent 1.0 ml ,sample or control 100 µl .

- mixed gently by inversion insert cuve he in to the cell holder and start stop watch.

-incubated for seconds and record initial absorbance reading .

-repeat the absorbance reading exactly after 1-2 and 3 minutes .

-calculate the difference between absorbance .

-calculate the mean of result to obtain the average change in absorbance per minute (ΔA/min). µ/l = ΔA/min x 1746 .

-the result are to be expresses as Si unit apply u/l x 0.01667= µ katal/l.

3.3.3 Normal range of Aspartate transaminase ;

Female up to 31 µ/l

Male up to 37 µ/l

3.4 Data analysis;

Data was analyzed using SPSS computer program . the means and standard deviation of plasma level of total cholesterol and aspartate transaminase(AST) activity were obtaine and the independent t. test user for comparison (P.value of ≤ 0.05) was considered significant.

chapter Foure

Results

Chapter four

Results

The levels of biochemical parameter of serum total cholesterol level and Aspartate transaminase (AST) activity in cigarette smokers and also compared with non cigarette smokers the result presented as follows;

Table (4.1) represent the mean of total cholesterol concentration (mg/dl) in cigarette smoker and control subject were significantly increase in cigarette smokers comparison with control values (211 mg/dl) and (154mg/dl) for smoker and control respectively (P.value =0.008).

Table (4.2) represent the mean of Aspartate transaminase (AST) activity (µ/l) in cigarette smoker and control subject were significantly increase in cigarette smokers comparison with control values (38 µ/l) and (23 µ/l) for smoker and control respectively (P.value =0.001)

Table (4.3) shows comparison of total cholesterol concentration (mg/dl) in cigarette smoker according to duration of cigarette smokers not significant change (2-10) years (more than11) years (213 mg/dl) and(227 mg/dl) (p value =0.007) respectively.

Table (4.4) shows comparison of total cholesterol concentration (mg/dl) in cigarette smoker according to number of cigarette per/day smokers not significant change (2-10) years (more than11) years (209 mg/dl) and (214 mg/dl)(p. value =0.000) respectively.

Table (4.5) show of comparison of total cholesterol concentration (mg/dl) in cigarette smoker according to age(18-45)years and (46- 86) years (211 mg/dl) (209mg/dl) (p.value=0.34)

Table (4.6) shows comparison of Aspartate transaminase (AST) activity in cigarette smoker according to duration of cigarette smokers not significant change (2-10) years (more than11) years (p .value =0.28) .

Table (4.7) shows comparison of Aspartate transaminase (AST)activity in cigarette smoker according to number of cigarette per/day smokers significant change (2-10) years (more than11) years (p.value =0.000) respectively.

Table (4.8) show of comparison of Aspartate transaminase (AST)activity in cigarette smoker according to age(18-45)years and (46- 86) years (p.value=0.16).

Figure (4.1) show that correlation between total cholesterol concentration (mg/dl) in cigarette smoker and duration of cigarette smokers. scatter plot showing r= 0.065 p.value =0.65 (weak positive correlation not significant)

Figure (4.2) show that correlation between total cholesterol concentration (mg/dl) in cigarette smoker and number of cigarette/day scatter plot showing r= 0.020 p.value =0.88 (weak positive correlation not significant)

Figure (4.3) show that correlation between total cholesterol concentration (mg/dl) in cigarette smoker and age of cigarette smokers scatter plot showing r=0.001 p.value =0.99 (weak positive correlation not significant) .

Figure (4.4) show that correlation between Aspartate transaminase (AST) activity in cigarette smoker and duration of cigarette smokers scatter plot showing r=- 0.005 p.value =0.97(weak negative correlation not significant)

Figure (4.5) indicated that correlation between Aspartate transaminase (AST) activity in cigarette smoker and number of cigarette/day scatter plot showing r=0.129.value =0.37 (weak correlation not significant) .

Figure (4.6) indicated that correlation between Aspartate transaminase (AST) activity and age of cigarette smokers .scatter plot showing r=0.0 65 p.value =0.0.65 (weak correlation not significant) .

Figure (4.7) show that correlation between total cholesterol concentration (mg/dl) in cigarette smoker and Aspartate transaminase (AST) activity in cigarette smoker scatter plot showing r= -0.20 p.value =0.15 (negative correlation not significant) .

Table (4.1)

The mean of total cholesterol concentration (mg/dl) in cigarette smokers and control subjects.

Subject group	Number	Mean ±SD	p.value
Smokers	50	211 ± 8.3	0.008
Control	50	154 ±5.4	

Result given mean ± SD

p.value $\leq$ 0.05considered significant.

Table (4.2)

The mean of Aspartate transaminase (AST) (µ/l) activity in cigarette smokers and control subjects.

Subject group	Number	Mean ±SD	p.value
Smokers	50	38 ±10	
Control	50	23 ±5.4	0.001

Result given mean ± SD

p.value ≤ 0.05considered significant.

Table (4.3)

The mean of total cholesterol concentration (mg/dl) in cigarette smokers according to duration of cigarette smokers.

Subject group	Number	Mean ±SD	p.value
2- 10 years	28	213 ± 4.8	0.007
More than 10 years	22	227 ± 9.3	

Result given mean ± SD

p.value ≤ 0.05considered significant.

Table (4.4)

The mean of total cholesterol concentration (mg/dl) in cigarette smokers according to number of cigarette/day.

Subject group	Number	Mean	±SD	p.value
2-10	28	209	± 5.7	
More than 11	22	224	± 8.4	0. 000

Result given mean ± SD

p.value ≤ 0.05considered significant.

Table (4.5)

The mean of total cholesterol concentration (mg/dl) in cigarette smokers according to age of cigarette smokers.

Subject group	Number	Mean ±SD	p.value
18-45 years	39	211 ± 5.5	
46-85years	11	209 ± 4.1	0.34

Result given mean ± SD

p.value ≤ 0.05considered significant.

Table (4.6)

The mean of Aspartate transaminase (AST) (µ/l) activity in cigarette smokers according to duration of cigarette smokers.

Subject group	Number	Mean ±SD	p.value
2- 10 years	28	38 ± 11	
More than10years	22	42 ± 9	0.28

Result given mean ± SD

p.value ≤ 0.05considered significant.

Table (4.7)

The mean Aspartate transaminase (AST) (µ/l) activity in cigarette smokers according to number of cigarette/day.

Subject group	Number	Mean ±SD	p.value
2-10	28	38 ± 10	
More than 11	22	42 ± 11	0. 88

Result given mean ± SD

p.value ≤ 0.05considered significant.

Table (4.8)

The mean of Aspartate transaminase (AST) (µ/l)activity in cigarette smokers according to age of cigarette smokers.

Subject group	Number	Mean ±SD	p.value
18-45 years	39	40 ± 11	0.16
46-85years	11	38 ± 8	

Result given mean ± SD

p.value ≤ 0.05considered significant.

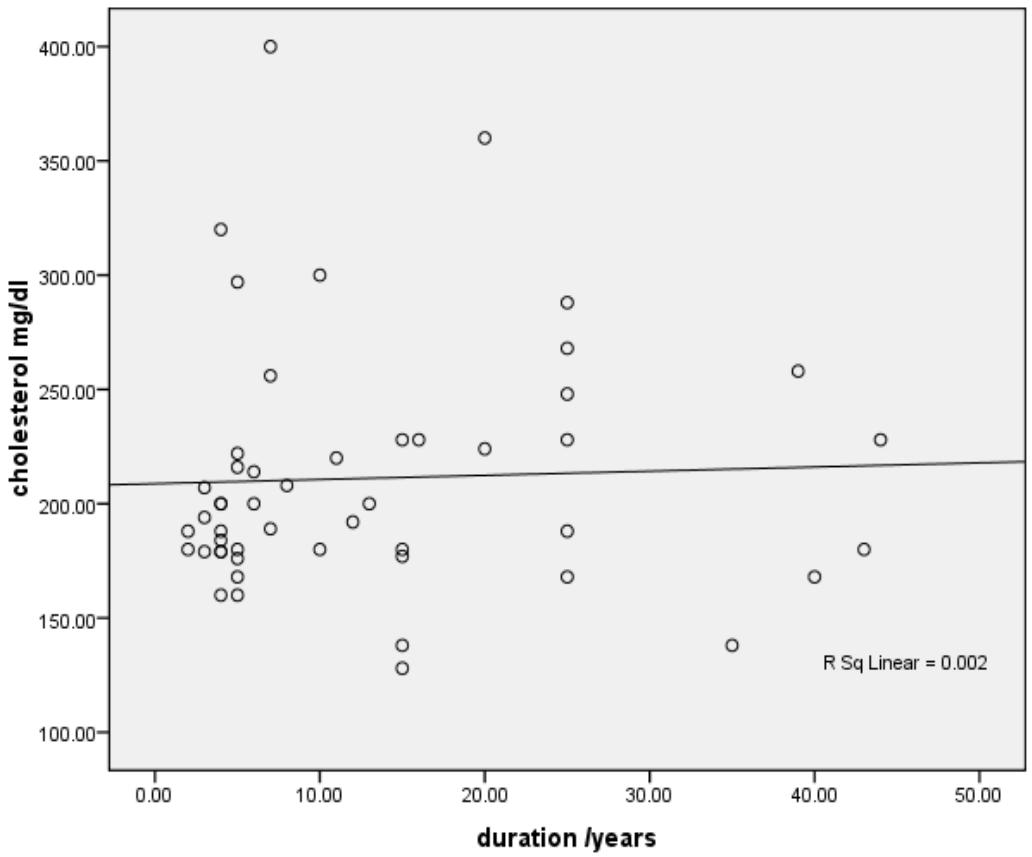


Figure (4.1)

Correlation between total cholesterol concentration (mg/dl) & duration of cigarette smokers.

A scatter plot shows the correlation between total cholesterol concentration (mg/dl) and duration of cigarette smoker r= 0.065 p.value =0.65

(weak positive correlation not significant) .

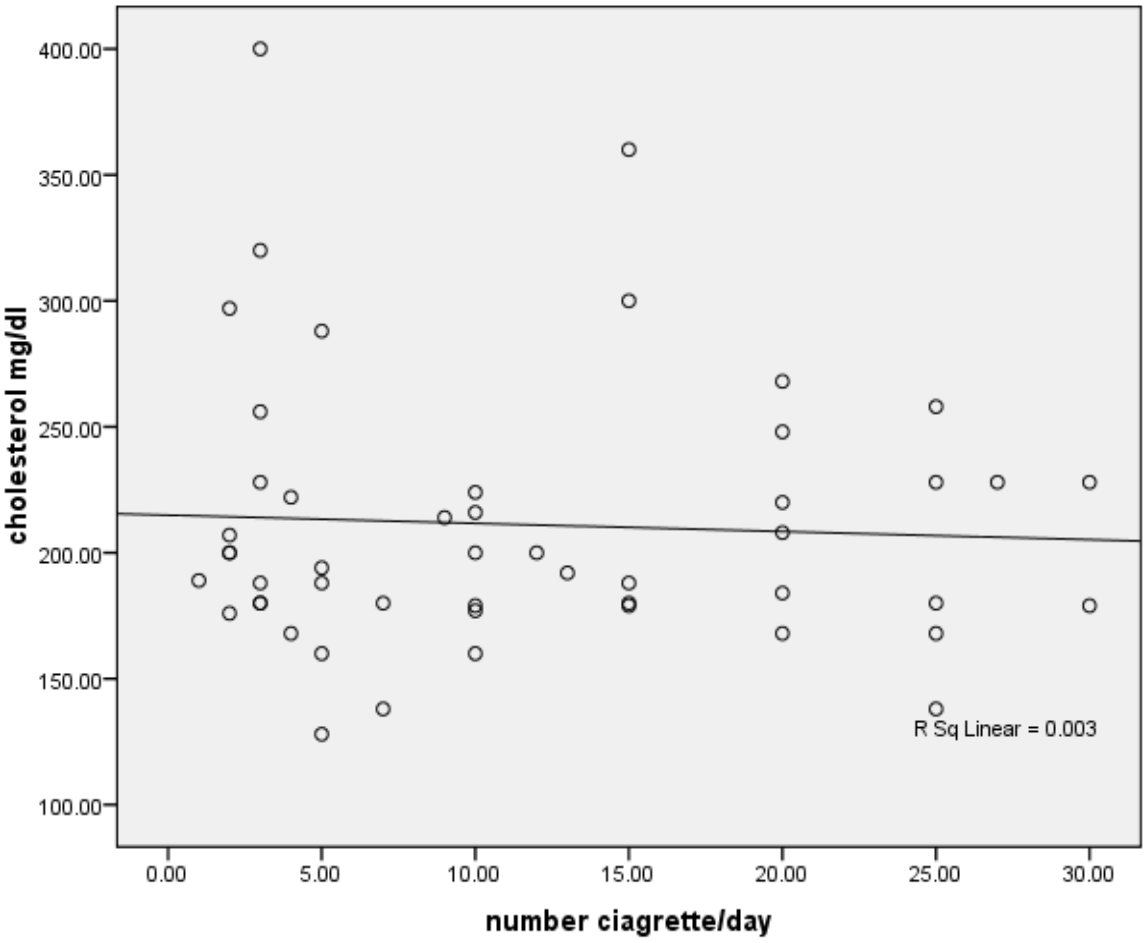


Figure (4.2)

Correlation between total cholesterol concentration (mg/dl) & number of cigarette/day of cigarette smokers.

A scatter plot shows the correlation between total cholesterol concentration (mg/dl) and number of cigarette per day r=0.020 p.value =0.88

(weak positive correlation not significant) .

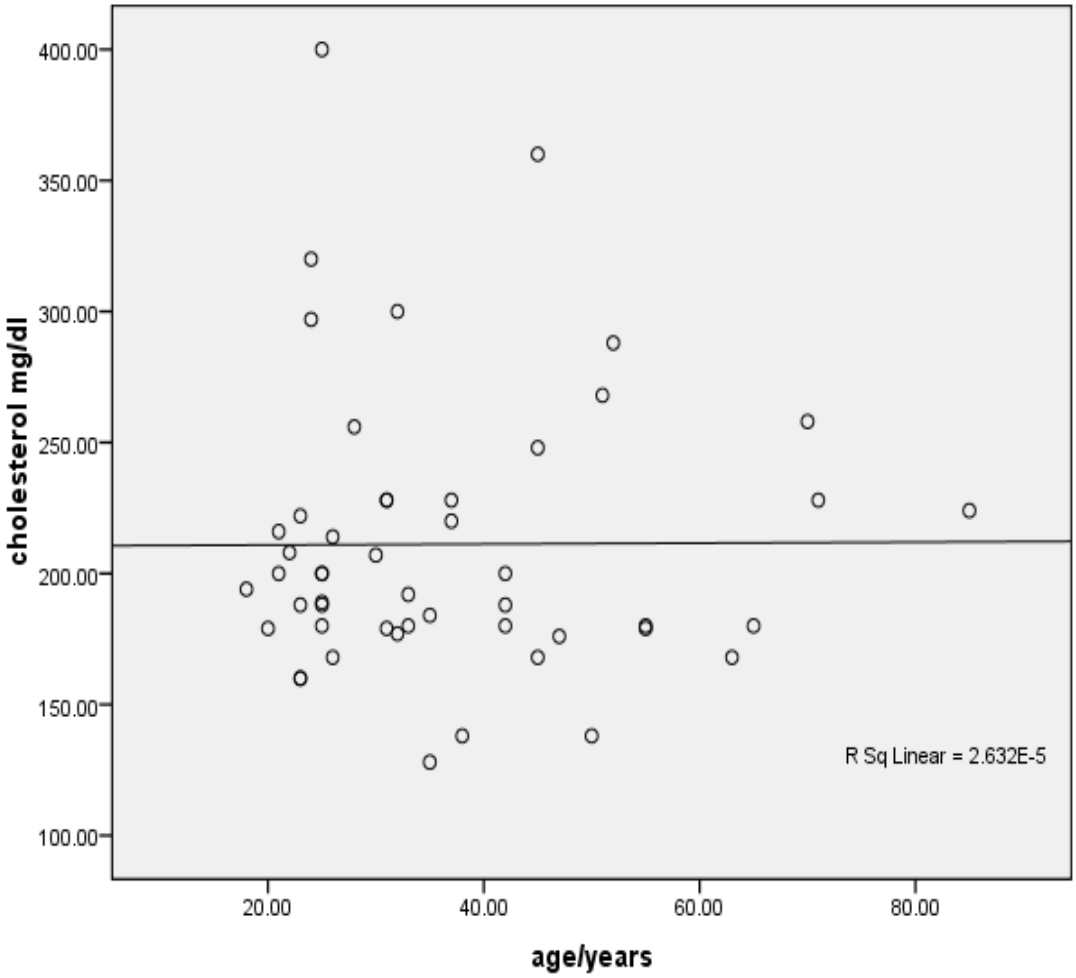


Figure (4.3)

Correlation between total cholesterol concentration (mg/dl) & age of cigarette smokers

A scatter plot shows the correlation between total cholesterol concentration (mg/dl) and age of cigarette smokers r=0.001 p.value =0.99 (weak correlation not significant) .

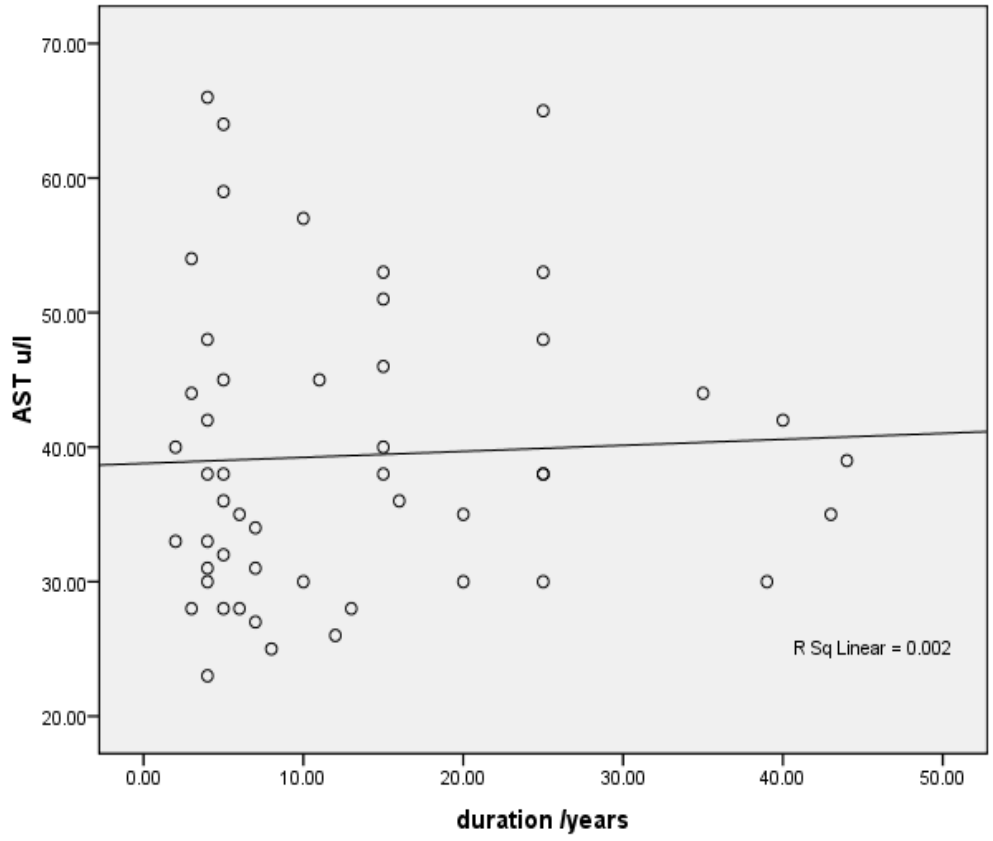


Figure (4.4)

Correlation between Aspartate transaminase (AST) (µ/l)activity & duration of cigarette smokers.

A scatter plot shows the correlation between Aspartate transaminase (AST) (µ/l) and duration of cigarette smoker r=-0.005 p.value =0.97

(weak correlation not significant) .

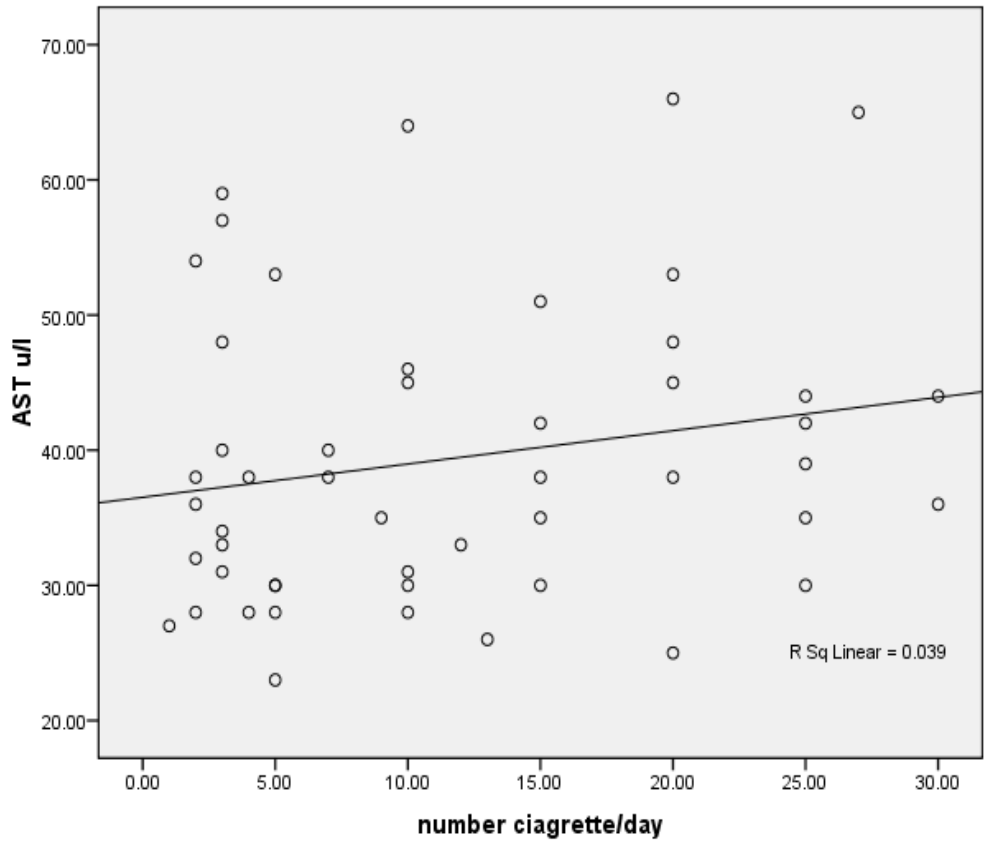


Figure (4.5)

Correlation between Aspartate transaminase (AST) (µ/l)activity & number of cigarette/day of cigarette smokers.

A scatter plot shows the correlation between Aspartate transaminase (AST) (µ/l) and number of cigarette smokers per/day r=0.129 p.value =0.37 (weak correlation not significant) .

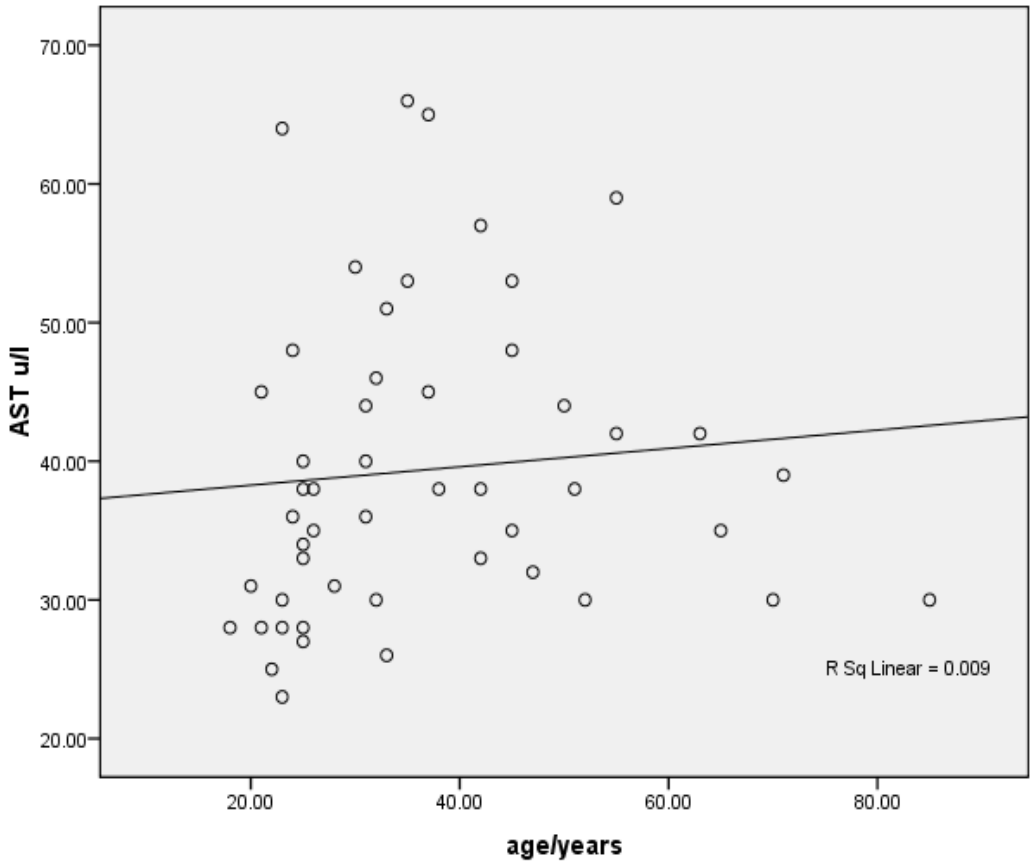


Figure (4.6)

Correlation between Aspartate transaminase (AST) (µ/l) activity& age of cigarette smokers .

A scatter plot shows the correlation between Aspartate transaminase (AST) (µ/l) and age of cigarette smokers r=0.065p.value =0.65
(weak correlation not significant) .

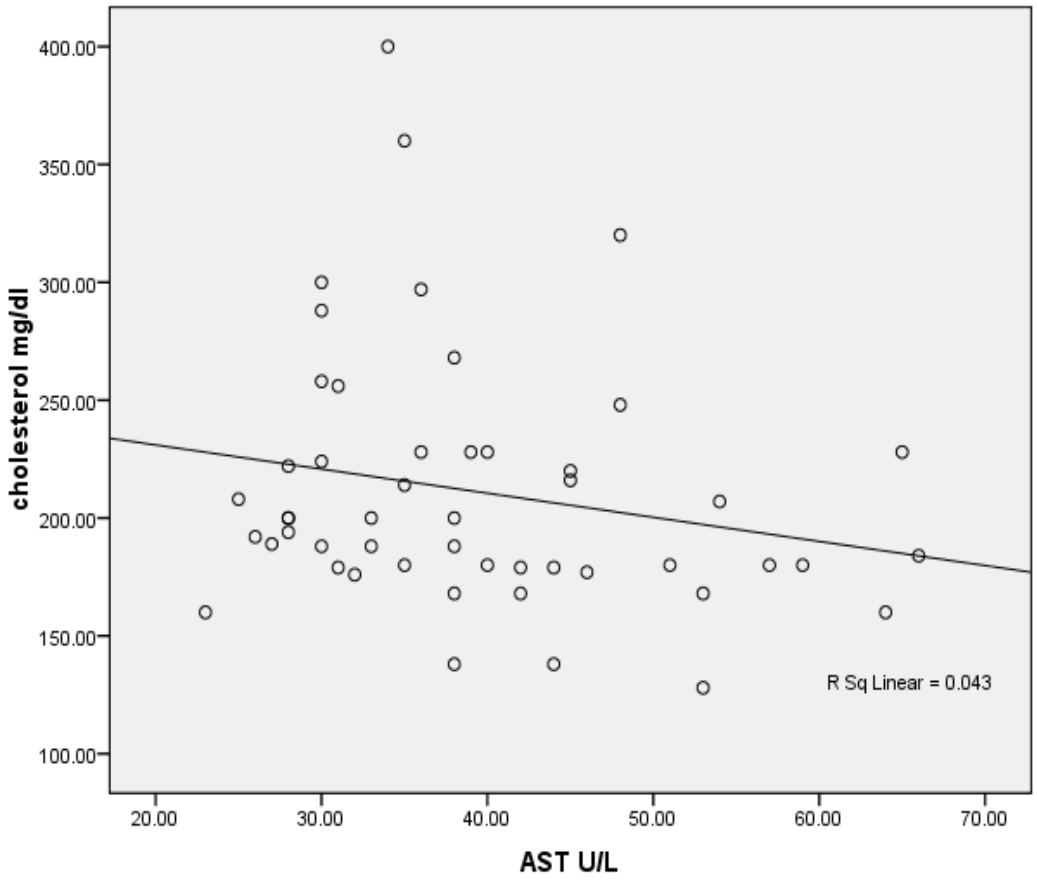


Figure (4.7)

Correlation between total cholesterol concentration (mg/dl) & Aspartate transaminase (AST) (µ/l) activity.

Ascatter plot shows the correlation between total cholesterol concentration transaminase (µ/l)and Aspartate r= -0.20 p.value =0.15

(negative correlation not significant) .

chapter Five

Discussion ,Conclusion and Recommendations

5.Chapter Five

5.1 Discussion

There are many evident that smoking is harmful and lead to death .world wide the effects of smoking are estimated to kill about 3 million per year .smoking in different forms is a major risk factor for atherosclerosis and coronary heart disease ,and there is a close relationship between the number of cigarette smoked and cardiovascular disease morbidity and mortality (Muscat &Harris 1991).

This study conducted to study the effect of smoking on the levels of total cholesterol and the enzyme Aspartate transaminase (AST) activity in male only with participate of female .because of know reason in Islamic country the male participant randomly selected are they representing different socioeconomic states(Altoum 2007) .

The results obtained from this study indicated that total cholesterol level in the blood of smokers showed 37% significant increase of the levels in the control non smokers the mean level in control was 154 mg/dl while it was 211 mg/dl in the smokers P.value was 0.008 at 0.05 level of significant these results are in agreement with the finding in(Altoum 2007)who claimed that cigarette smoking caused increase in the level of the total cholesterol by (Belot 1995) who observed increase lipid profile in the blood smokers.

When investigating the effect of the duration of smoking ,age smoker and number of cigarette smoked per day, on total cholesterol level it appeared that there is significant increase in the level of total cholesterol individual who under smoked of duration of more than ten years than smokers who under ten years than smoking mean level of total cholesterol level

2-10 years (213±4.8) more than 11years (227±9.3)mg/dl with p.value (0.007) and means of Aspartate transaminase(AST) activity 2-10 years (38± 11) µ/l more than11 years (42±9) µ/l with p.value =(0.28 .)

the number of cigarette per day must be found effect the level of total cholesterol is significant increase in the level of total cholesterol in the blood of smokers who smoked more than 10 cigarette than smoker less than 10 the age of the smokers Mean 2-10 cigarette/day (209±5.7) mg/dl more than 11cigarette /day (224±8.4) mg/dl p.value =0.0000 2-10 cigarette/day (38±10) µ/l more than 11cigarette /day (42±11) µ/l p.value =0.88 respectively.

was found not affect the level of total cholesterol in that subject of ages group Mean in 18- 45 years (211±5.5) mg/dl 46- 85years (209±4.1) mg/dl with p.value (0.34) maintain the same level of total cholesterol as in group 18-45 years 46 -86 years no significant differences' between the value of total cholesterol in two group of ages these result are also was reported by a there workers, example(Mjos1988),(Muscat &Harris 1991) observe the increase lipid profile in total cholesterol level in blood of smokers, this finding also confirm by Altoum (2007).

Positive correlation between lipid profile and duration of cigarette smoking was also reported(Muscat & Haris1991) claimed that the level of total cholesterol level in the blood of the smokers increase with the increase of the number of smoked cigarette ,recently Altoum (2007) observed strong correlation between the level of total cholesterol in the blood of the smoker and number of cigarette smoked.

The study also showed that the enzyme Aspartate transaminase (AST) activity was significant increase in blood of the smokers with p.value 0.001at 0.05 level of significancy .A number of about 69% over control value was attained

Aspartate transaminase (AST) ativity An enzyme know to be associated with heart disease and pulmonary embolism it useful assay for myocardial infarction . Since the enzyme activity was fund increase sharply within the first 12 hours with a peak level at 24 hours or over and return to normal within 3to 5 days.

The enzyme Aspartate transaminase (AST) activity measured in the blood of the smoker in rolled in these study also was fund not to be affected by the duration of smoking nor with the number of cigarette smoked per day or the age of smokers , (p.value were above 0.05).

When assessing any correlation between the two parameters (total cholesterol level and Aspartate transaminase activity) measure in this study was observed no correlation between total cholesterol level and Aspartate transaminase (AST)activity .

The result of this is study are in agreements of a there worker s on total cholesterol as well as triglyceride and LDL was remarkable reduction in HDL level in a there ward smoking of any forma con alter lipid profile an can cause grave consequence .alteration of lipid profile can adversely causing dyslipidiaemia in smokers and the changes become more mark with the increase number of cigarette smoked and with the increase of the duration of smoking in years ,smoking cause an increase in oxidize LDL cholesterol level which plays the key role for a atherosclerotic process A high levels of LDL-C ,and triglyceride are strongly associated with the development of

coronary artery disease while a low level of HDL-C remains asiginificant independent predictor of coronary artery disease.
(EPRNCEP& Simonetta 1991).

5.2 Conclusion

Frome the result and findins in the is study it is conceded that ;

1-Total cholesterol and Aspartate transaminase(AST) activity significant elevated in the blood of Sudanese smokers in roll in this study mean compare non smokers

2-Total cholesterol level was found affected by the duration of smoking and number of cigarette smoked .

3- The age of smokers has no significance the level of total cholesterol .

4-The level ofAspartate trasaminase (AST) activity has being found not to be affected by the duration of smoking nor in the number cigarette per day or age of smokers.

5.3 Recommendations

1- All those working in the medical field must participate in advising the community about the dangerous of cigarette smoking.

2- Health education for the community to know the hazard and complication of cigarette smokers.

3-more parameters should be studied to cover the effects of cigarette smoking on body health.

4- Generalization of the most effective international plans to reduce smoking among population.

5-The government must play an obvious role is the war against cigarette smokers.

6-Lipid profile should be regularly monitor in the blood of heavy smoker to detected to hazard to cardiovascular and atherosclerosis.

7- heavily smoker should be advice to cute of or reduce the number of cigarette per day .

8- Dangerous of smoking as adapt anal of mortality and morbidity mast be firm ally in forces by all media .

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APPENDIXES

Sudan University of science and technology

Collage of graduate students

Questionnaire

Master degree

Determination of serum cholesterol and Aspartate transaminase in cigarette ;smokers in Khartoum state

……Name

……Age

..…… Duration of smoking

……Number of cigarettes/day

.S .total cholesterol level ……mg/dl

S.Asprartate trasaminase Activity ……µ/L